

**Preliminary Amendment**

Prior to examining the elected claims on the merits, please amend the application as follows.

**In the Claims:**

Please cancel claims 2-38 and 41-57, without prejudice to including the subject matter of the canceled claims in one or more additional patent applications.

Please amend claim 39 to read as follows. For the Examiner's convenience, a "Marked-Up Copy of Claim Amended" is included herewith, in which text added to the claim is underlined and text deleted from the claim is struck-through. The Applicants have also included a "Clean Copy of Claims, as Amended," in which all claims pending after entry of this Response and Preliminary Amendment are listed in an order which the Applicants believe is appropriate for issue.

Please amend claim 39 to read as follows.

39. (Amended) A method of selecting a dose of an anti-oxidant composition for administration to a human, the method comprising assessing occurrence in the human's genome of disorder-associated polymorphisms in at least two genes selected from the group consisting of

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- a) genes which encode an enzyme that catalyzes conversion of a toxic oxygen species to a less toxic oxygen species;
  - b) genes which encode a protein that provides protection against oxidative stress;
  - c) genes which encode a protein that induces production of a toxic oxygen species;
  - d) genes which encode a protein that indirectly affects oxidative stress; and
  - e) genes which encode a protein for which the level of expression of the protein is associated with oxidative stress,

whereby occurrence of any of the polymorphisms is an indication that a greater dose of the composition should be administered to the human; and

selecting a dose of the composition based on occurrence of the polymorphisms.

Please add claim 58-94 as follows.

~~58. The method of claim 39, wherein the genes are selected from the group consisting of a), b), c), and d).~~

~~59. The method of claim 39, wherein the genes are selected from the group consisting of a), b), and c).~~

60. The method of claim 39, comprising assessing occurrence in the human's genome of disorder-associated polymorphisms in at least four genes selected from the group consisting of genes which encode an enzyme that catalyzes conversion of a toxic oxygen species to a less toxic oxygen species.

61. The method of claim 60, wherein the genes are

- i) the gene which encodes mitochondrial manganese superoxide dismutase (MnSOD),
- ii) the gene which encodes cytoplasmic copper/zinc superoxide dismutase (CZSOD),
- iii) the gene which encodes catalase, and
- iv) the gene which encodes glutathione peroxidase.

62. The method of claim 39, wherein the genes are selected from the group consisting of

- i) the gene which encodes MnSOD,
- ii) the gene which encodes CZSOD,
- iii) the gene which encodes catalase,
- iv) the gene which encodes glutathione peroxidase,
- v) the gene which encodes glutathione S-transferase,
- vi) the gene which encodes glutathione reductase,
- vii) the gene which encodes thioredoxin reductase,
- viii) the gene which encodes paraoxonase,
- ix) the gene which encodes NAD(P)H:quinone oxidoreductase 1,
- x) the gene which encodes 8-oxo-7,8-dihydrodeoxyguanosine triphosphatase,

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- xi) the gene which encodes epoxide hydrolase,
  - xii) the gene which encodes myeloperoxidase,
  - xiii) the gene which encodes tumor necrosis factor alpha,
  - xiv) the gene which encodes NADH/NADPH oxidase p22 phox protein,
  - xv) the gene which encodes nitric oxide synthase
  - xvi) the gene which encodes xanthine oxidase,
  - xvii) the gene which encodes cytochrome P450,
  - xviii) the gene which encodes apolipoprotein E,
  - xix) the gene which encodes UDP-glucuronosyltransferase 1A1,
  - xx) the gene which encodes acid phosphatase,
  - xxi) the gene which encodes protein phosphotyrosine phosphatase,
  - xxii) the gene which encodes epinephrine oxidase,
  - xxiii) the gene which encodes cystathionine beta-synthase,
  - xxiv) the gene which encodes cystathionine gamma-lyase,
  - xxv) the gene which encodes N5-methyl THF:homocysteine methyltransferase,
  - xxvi) genes which encode an S-adenosylmethionine methyltransferase, and
  - xxvii) genes which encode a heat shock protein.

63. The method of claim 62, wherein the genes are selected from the group consisting of i) through iv).

64. The method of claim 62, wherein the genes are selected from the group consisting of i) through xi).

65. The method of claim 62, wherein the genes are selected from the group consisting of i) through xvii).

66. The method of claim 62, comprising assessing occurrence in the human's genome of disorder-associated polymorphisms in at least four of i) through xxvii).

67. The method of claim 62, comprising assessing occurrence in the human's genome of disorder-associated polymorphisms in at least six of i) through xxvii).

68. The method of claim 62, comprising assessing occurrence in the human's genome of disorder-associated polymorphisms in at least ten of i) through xxvii).

69. The method of claim 62, comprising assessing occurrence in the human's genome of disorder-associated polymorphisms in at least fifteen of i) through xxvii).

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70. The method of claim 39, wherein occurrence of an individual disorder-associated polymorphism is assessed by  
contacting a nucleic acid derived from the human's genome with a first oligonucleotide that anneals with higher stringency with the disorder-associated polymorphism than with a corresponding non-disorder-associated polymorphism and  
assessing annealing of the first oligonucleotide and the nucleic acid,  
whereby annealing of the first oligonucleotide and the nucleic acid is an indication that the human's genome comprises the disorder-associated polymorphism.

71. The method of claim 70, wherein the first oligonucleotide is attached to a support.

72. The method of claim 71, wherein the support has a plurality of different first oligonucleotides attached thereto.

73. The method of claim 72, wherein the support has attached thereto at least five first oligonucleotides that anneal with higher stringency with the disorder-associated polymorphisms than with the corresponding non-disorder-associated polymorphisms.

74. The method of claim 72, wherein the support has attached thereto at least ten first oligonucleotides that anneal with higher stringency with the disorder-associated polymorphisms than with the corresponding non-disorder-associated polymorphisms.

75. The method of claim 72, wherein the support has attached thereto at least fifteen first oligonucleotides that anneal with higher stringency with the disorder-associated polymorphisms than with the corresponding non-disorder-associated polymorphisms.

76. The method of claim 70, wherein the first oligonucleotide is a molecular beacon oligonucleotide.

77. The method of claim 70, wherein occurrence of an individual disorder-associated polymorphism is further assessed by

contacting the nucleic acid with a second oligonucleotide that anneals with higher stringency with a non-disorder-associated polymorphism than with the corresponding non-disorder-associated polymorphism and

assessing annealing of the second oligonucleotide and the nucleic acid, whereby annealing of the second oligonucleotide and the nucleic acid is an indication that the human's genome does not comprise the disorder-associated polymorphism.

78. The method of claim 77, wherein the second oligonucleotide is attached to a support.

79. The method of claim 78, wherein the first and second oligonucleotides are attached to the same support.

80. The method of claim 77, wherein the second oligonucleotide is a molecular beacon oligonucleotide.

81. The method of claim 70, wherein the first and second oligonucleotides are spectrally distinct molecular beacon oligonucleotides.

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82. The method of claim 39, further comprising calculating a susceptibility score by summing, for each of the selected genes in which a disorder-associated polymorphism occurs in the human's genome, the product of a constant and a correlation factor, wherein the correlation factor represents the fraction of humans heterozygous or homozygous for the disorder-associated polymorphism who exhibit the corresponding disorder, whereby the susceptibility score represents the relative susceptibility of the human to oxidative damage.

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83. The method of claim 82, wherein the same constant is used for each selected gene.

84. The method of claim 82, wherein the constant used for each gene of group a) is greater than the constant used for the genes of groups b), c), d), and e).

85. The method of claim 84, wherein the constant used for each gene of group a) is at least twice as great as the constant used for the genes of groups b), c), d), and e).

86. The method of claim 85, wherein the genes are selected from the group consisting of a), b), and c).

87. The method of claim 86, wherein the genes are selected from the group consisting of

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- i) the gene which encodes MnSOD,
  - ii) the gene which encodes CXSOD,
  - iii) the gene which encodes catalase,
  - iv) the gene which encodes glutathione peroxidase,

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- v) the gene which encodes glutathione S-transferase,
  - vi) the gene which encodes glutathione reductase,
  - vii) the gene which encodes thioredoxin reductase,
  - viii) the gene which encodes paraoxonase,
  - ix) the gene which encodes NAD(P)H:quinone oxidoreductase 1,
  - x) the gene which encodes 8-oxo-7,8-dihydrodeoxyguanosine triphosphatase,
  - xi) the gene which encodes epoxide hydrolase,
  - xii) the gene which encodes myeloperoxidase,
  - xiii) the gene which encodes tumor necrosis factor alpha,
  - xiv) the gene which encodes NADH/NADPH oxidase p22 phox protein,
  - xv) the gene which encodes nitric oxide synthase
  - xvi) the gene which encodes xanthine oxidase, and
  - xvii) the gene which encodes cytochrome P450.

88. The method of claim 87, comprising assessing occurrence in the human's genome of disorder-associated polymorphisms in at least four of i) through xvii).

89. The method of claim 87, comprising assessing occurrence in the human's genome of disorder-associated polymorphisms in at least six of i) through xvii).

90. The method of claim 87, comprising assessing occurrence in the human's genome of disorder-associated polymorphisms in at least ten of i) through xvii).

91. The method of claim 87, comprising assessing occurrence in the human's genome of disorder-associated polymorphisms in at least fifteen of i) through xvii).

92. The method of claim 39, wherein each of the polymorphisms is a single nucleotide polymorphism (SNP).

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93. The method of claim 92, wherein occurrence of a SNP is assessed by annealing a nucleic acid derived from the human's genome with a primer that is complementary to the region adjacent the SNP on its 3' side, extending the primer using a polymerase in order to add a nucleotide residue complementary to the SNP to the primer, and detecting the identity of the nucleotide residue complementary to the SNP.

94. The method of claim 93, wherein the nucleotide residue is a non-extendable residue. --

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### REMARKS

Claims 1, 39, 40, and 58-94 are pending following entry of this Preliminary Amendment. Claims 1, 39, and 40 are the only independent claims.

Claims 1 and 40 stand withdrawn from consideration. Claims 2-38 and 41-57 have been canceled without prejudice. Claim 39 has been amended. Claims 58-94 have been added. Amended claim 39 is supported by originally filed claim 1. Newly added claims 58-94 are supported by (and substantially mirror) originally filed claims 2-38.

No additional fee is believed to be due corresponding to filing of this Response, because it is being filed on or prior to the deadline (November 2, 2002) for responding to the Restriction Requirement and because no additional claim fees are believed to be due (54 claims having been canceled and 37 dependent claims having been added). In the event an additional fee is due, please charge the fee (or credit any overpayment) to Deposit Account No. 50-1017 (Billing No. 210691.0001).

Claims 39 and 58-94 correspond to Group II identified by the Examiner in the Restriction Requirement.